

Microdroplet lasers and their applications

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Abstract. Bio-integrated lasers, that are lasers made of biological and biocompatible materials and implanted into cells and tissues, are gaining interest from the research community. Here we show how whispering gallery mode microlasers and microcavities made of solid beads or droplets can be used for sensing different processes in biological materials including inside cells. By making microcavities of a predefined size they can also be used to encode some information and for cell tracking. Sensing and tracking can be applied to highly scattering tissues.

Currently the most frequently used techniques to study complex processes in live cells employ fluorescent probes. However, fluorescent probes have several disadvantages including photobleaching, sensitivity to environmental factors and broad emission spectrum, which limits their sensitivity, multiplexing ability and imaging capabilities in biological tissues. The transition from detecting laser emission from bio-integrated lasers instead of fluorescence represents a paradigm shift. Due to narrow emission linewidth, high coherence, large intensity and highly nonlinear output from lasers, they open huge opportunities in ultrasensitive sensing, spectral multiplexing and microscopy.

Micro-sized lasers completely embedded within single live cells [1] and biological tissues [2] have been demonstrated. The lasers were made out of solid beads and droplets including biocompatible and biodegradable materials. We have observed that both macrophages and non-macrophage cells engulf beads up to 20 μm in diameter (Fig. 1a). The lasers inside cells can act as very sensitive sensors, enabling us to better understand cellular processes. By using a micro pipette droplets of high refractive index oil containing fluorescent dye were injected into a cell. By analyzing the light emitted by a droplet laser, we can measure that deformation and calculate the forces acting within a cell (Fig. 1b).

Further, lasers were used for cell tagging. Each laser within a cell emits light with a slightly different fingerprint that can be easily detected and used as a barcode to tag the cell [3], providing the ability the study cell migration. By using a micro pipette droplets of high refractive index oil containing fluorescent dye were injected into a cell. By injection the diameter of the generated oil droplets and polymerized microbeads could be reproduced with a standard deviation of 1 nm and 20 nm, respectively. Encoding of short words and numbers has been demonstrated by producing three beads with

predefined sizes (Fig. 1c) [4]. The stored information has been read from the emitted spectrum.

Droplet lasers serve as well to precisely measure interfacial tension between to immiscible liquids [5]. The interfacial tension is calculated from the Young–Laplace equation where the radius and the internal pressure needs to be measured. The size of the droplet is monitored and pressure is applied to the microcapillary to measure the equilibrium pressure (Fig. 1d). The droplet shown in Fig. 1d has an equilibrium pressure of 1.75 kPa. With this method it is possible to measure interfacial tension of volumes in the picoliter range.

We have also demonstrated that small lasers can be used for novel nonlinear microscopy, including super resolution imaging [6] and imaging in highly scattering tissues [7]. When the lasers are embedded into deep into the tissue, because of scattering their image is blurred (Fig. 1e and f). Since the spectral positions of laser lines do not change with propagation through scattering and absorbing media, we are still able to measure their spectrum (Fig. 1g). From the spectrum we can determine the number of microcavities embedded in the tissue, their individual sizes and the surrounding refractive index. The size can be used for previously mentioned barcoding. For sensing the beads are functionalized with a coating which changes the refractive index based on the change in the environment, such as temperature and pH. Simultaneously we can also measure the position of each laser in all three dimensions. Even though the image of closely separated lasers is highly blurred (Fig. 1f), we can extract the contribution of each laser by capturing their unique spectra (Fig. 1g). Therefore, the contribution of each laser to the final image can be isolated and position can be determined. This is similar to PALM or STORM, but the signal of each emitter is not separated in time but in spectrum.

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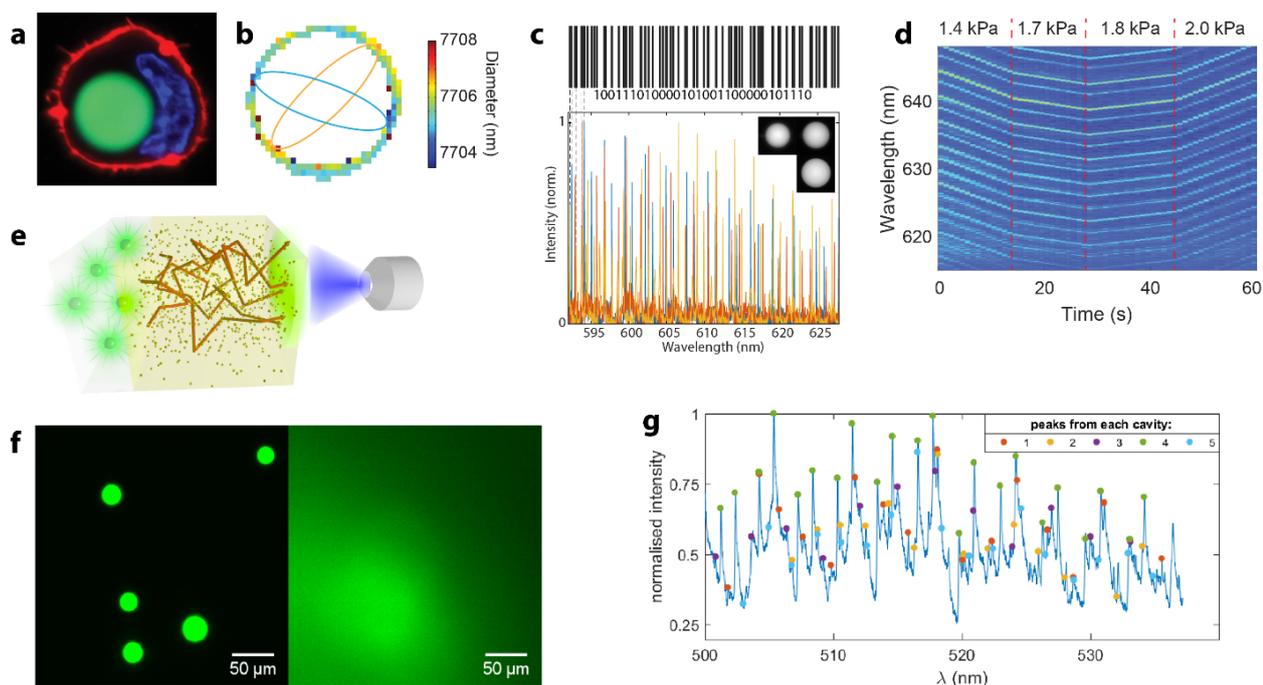


Fig. 1. a) Laser inside a cell. b) Diameter map shows deformation of the cavity. c) Spectra collected from three beads with predefined sizes. The sizes of the three generated beads calculated from their spectrum encode the word “STEFAN” which is written as a binary number. d) Change of the spectrum as the pressure to the droplet is changed. e) Scattering of light from lasers embedded in a scattering tissue. f) Microcavities without and with scattering layer on top. g) From the spectrum the size, surrounding refractive index and position of each microcavity can be determined.

Lasers made from liquid crystals which emit vector beams were also studied. Liquid crystals form an extremely rich range of self-assembled topological structures with artificially or naturally created topological defects. Liquid crystals have been used before inside laser cavities, however, until now only relatively simple liquid-crystal structures have been employed. Our study provides experimental and simulation insights into coupling of light with the complex liquid-crystal topological superstructures inside a laser cavity [8]. This results in non-trivial intensity and polarization of the generated structured light. The proposed soft matter microlaser approach opens new direction in soft matter photonics research.

Lasers made of soft and biological materials including liquids and integrated into the living biological systems have potential to enable novel applications including sensing and imaging [9,10].

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